

## Original Article

# Analysis on correlation of white matter lesion and lacunar infarction with vascular cognitive impairment

Ting Yan<sup>1\*</sup>, Jia-Rui Yu<sup>1\*</sup>, Yun-Pei Zhang<sup>1</sup>, Tao Li<sup>2</sup>

<sup>1</sup>Department of Imaging, The Third Hospital of Ji Nan, Shandong, China; <sup>2</sup>Department of Neurology, The Fourth Hospital of Ji Nan, Shandong, China. \*Co-first authors.

Received May 6, 2015; Accepted July 28, 2015; Epub August 15, 2015; Published August 30, 2015

**Abstract:** Objective: To investigate the correlation of white matter lesion (WML) and lacunar infarction (LI) with vascular cognitive impairment. To investigate the correlation of cognitive changes of vascular dementia (VD) patients with lacunar infarction (LI) and white matter lesion (WML). Methods: The clinical data of 60 cases of VD patients were evaluated and analyzed by combining with imageological findings and cognitive function assessment. Results: Multiple LI and WML were negatively correlated with both mini-mental state examination (MMSE) scale scores ( $r = -0.401$ ,  $P = 0.036$ ) and clock drawing test (CDT) scale scores ( $r = -0.482$ ,  $P = 0.028$ ); the LI number in occipital lobe was negatively correlated with MMSE scores ( $r = 0.338$ ,  $P = 0.048$ ), the LI number in temporal lobe was negatively correlated with CDT scores ( $r = -0.235$ ,  $P = 0.047$ ), and the LI number in frontal lobe was negatively correlated with MoCA scores ( $r = -0.450$ ,  $P = 0.039$ ). Conclusion: All of LI location and number as well as WML are independent influencing factors of cognitive impairment of VD patients.

**Keywords:** White matter lesion, multiple lacunar infarction, vascular cognitive impairment

## Introduction

Vascular dementia (VD), as a relatively severe cognitive impairment, usually occurs in older people. The prevalence rate of vascular dementia is 5% in those over 65. It has a morbidity second only to Alzheimer's disease regarding the proportion in senile dementia [1]. The risk factors including cerebrovascular disease hypertension, hyperlipidemia arteriosclerosis [2]. The common causes include ischemic or hemorrhagic stroke and other ischemic white matter lesions leading to cerebral ischemia or hypoxia [3, 4]. Of them, the most common cause is ischemic stroke (also known as cerebral infarction), whose most common pathogenic factor is believed to be atherosclerosis [5, 6]. Ischemic infarction occurring in cerebral small arteries will gradually heal with time and eventually form irregular lacunae, thus developing the condition called lacunar infarction (LI). At present, a large number of studies have confirmed the important correlation of LI and white matter lesion (WML) with VD [7, 8].

Both LI and WML can be imageologically observed directly by using brain magnetic reso-

nance imaging (MRI) or other means, which leads some scholars to consider whether these two items play a predictive role for VD [9]; however, this idea remains inconclusive so far. It has been demonstrated that both the number and location of imageologically observed LIs exert an influence on patient's cognitive function, especially when LIs are found in such sites as thalamus and putamen. Nevertheless [10], it remains controversial whether there is an established relationship between WML and cognitive changes [11]. Therefore, this study is designed to investigate the correlation of VD patients with multiple lacunar infarction and cerebral WML.

## Materials and methods

### Object

Sixty cases of VD patients admitted to Neurology Department of our hospital from January 2011 to January 2013 were diagnosed according to the symptoms, signs, imageological evidence and status of cognitive dysfunction, and their clinical data was then analyzed. These are 25 males and 35 females aged from 50 to 78

**Table 1.** Correlation of LI Location with MMSE, CDT and MoCA Scores ( $\bar{x} \pm s$ )

	LI number	MMSE (points)	CDT (points)	MoCA (points)
Cortex	0.93±0.89	24.33±3.54	3.41±0.47	22.14±3.43
r/P value		-1.248/0.145	0.450/0.695	-0.053/0.897
Temporal lobe	1.00±0.33	24.55±3.33	3.43±0.41	21.24±3.65
r/P value		-0.028/0.756	-0.235/0.047	-0.058/0.778
Parietal lobe	2.00±1.14	24.57±3.68	3.49±0.51	22.14±4.46
r/P value		-0.036/0.792	0.057/0.782	0.233/0.253
Frontal lobe	2.25±1.43	22.89±2.45	3.21±0.91	20.15±3.88
r/P value		0.025/0.890	-0.096/0.644	-0.450/0.039
Occipital lobe	0.83±0.24	23.56±3.98	3.36±0.31	23.14±5.29
r/P value		0.338/0.048	0.243/0.403	0.403/0.267
Basal ganglia	0.97±0.34	25.51±2.89	3.26±0.31	20.46±2.99
r/P value		-0.027/0.852	0.116/0.524	-0.188/0.302

[mean age (63.36±10.01)] years; their MMSE scale scores were (24.53±3.62) points, CDT scores were (3.46±0.51) points and MoCA scores were (21.51±3.49) points. In terms of WML grade, Grade 0 was reported in 12 cases (20.0%), Grade 1 in 28 cases (46.7%), Grade 2 in 14 cases (23.3%), and Grade 3 in 6 cases (10.0%), with an average of Grade (1.53±1.64). This study was conducted in accordance with the declaration of Helsinki. This study was conducted with approval from the Ethics Committee of Jin Nani First People's Hospital. Written informed consent was obtained from all participants.

The total number of lacunar infarction sites was 479, including 56 sites in cortex, 60 in temporal lobe, 120 in parietal lobe, 135 in frontal lobe, 50 in occipital lobe and 58 in basal ganglia. Inclusion criteria: Either multiple LI or WML or both found by MRI; only mild cognitive impairment. Exclusion criteria: Patients with any of the following conditions were excluded: dysfunction or degradation of vital organs like heart, liver, lung and kidney; diabetes, hypertension and other chronic diseases; severe mental illness; macrovascular diseases in brain; any of previous history of cerebral hemorrhage.

The detection indicators included general information [age, gender, body mass index (BMI), etc.], blood routine, blood biochemistry, neuropsychiatric inventory (including MMSE, CDT and MoCA), LI number and WML (evaluated by MRI or MRA), etc. The total scores of MMSE were 30 points; the total scores of CDT were 4 points,

which primarily aimed to reflect the visual-spatial, planning and other functions in the scope of cognition; the total scores of MoCA were 30 points, which were designed to observe the memory, attention and executive ability in patient cognitive function; WML was classified into 0~3 grades according to Fazekas scale [12].

#### Statistical methods

Software SPSS19.0 was used for the linear regression analysis.

## Results

### Correlation between WML and cognitive function

WML was negatively correlated with both MMSE scores ( $r = -0.401$ ,  $P = 0.036$ ) and CDT scores ( $r = -0.482$ ,  $P = 0.028$ ) while was not significantly correlated with MoCA ( $r = -0.123$ ,  $P = 0.682$ ).

### Correlation between lacunar infarction and cognitive function

The LI number in occipital lobe was negatively correlated with MMSE scores ( $P = 0.048$ ), the LI number in temporal lobe was negatively correlated with CDT scores ( $P = 0.047$ ), and the LI number in frontal lobe was negatively correlated with MoCA scores ( $P = 0.039$ ); no significant difference was reported in other correlations (Table 1).

## Discussion

In the causes of VD patients, cerebral small vessel diseases are gaining an increasing proportion, and some studies even state that such diseases have become the primary cause of VD [13]. Despite of the extensive application of imageological evidence like MRI in studies regarding cerebral physical and mental activities, the subjective cognitive function of patients cannot be obtained from the imageological evidence yet [14, 15]. MMSE scores have been widely used in the therapies of neurology department owing to the advantages of

simple operation and high accuracy and sensitivity; however, the simple operation also leads to a rough rather than detailed evaluation of patient's cognitive function [16]. When evaluating patient's cognitive function, CDT scores mainly cover visual-spatial and planning functions as well as the executive function [17]. Inversely, MoCA scale is featured with high sensitivity and specificity and plays an important role in the diagnosis and assessment of vascular causes that lead to cognitive impairment. The results of this paper suggest that LI location and number are closely associated with cognitive function in VD patients, which is independent from cerebral WML [18]. LIs in frontal lobe will lead to reduced MoCA scores and mainly interfere with patient memory function. Based on the assessment of MoCA scores on delayed memory in the scope of episodic memory and by combining with anatomical theory, the medial temporal lobe, frontal lobe and nucleus anterior thalami are mainly responsible for human episodic memory function, where frontal lobe tends to code and manage information [19]. The findings are consistent with the anatomical structure. Occipital lobe is mainly responsible for processing physical visual information, and their effect on the correlation with cognitive function appears to be not significant. Temporal lobe not only exerts an important impact on memory function together with frontal lobe but also is responsible for processing auditory information and managing emotions. Consequently, the LI number in temporal lobe will affect CDT scores, suggesting a significant correlation between them [20].

The results of the study demonstrate that cerebral WML may result in patient's cognitive impairment to varying degrees. All of LI location and number as well as WML are independent influencing factors of cognitive impairment of VD patients [21, 22]. However, given the small number of samples included in this study, more large-scale and long-term clinical studies are required to verify the conclusion.

### Disclosure of conflict of interest

None.

**Address correspondence to:** Yun-Pei Zhang, Department of Imaging, Jin Nani First People's Hospital, Shandong, China. Tel: +86 531 88985434;

Fax: +86 531 88985434; E-mail: yunpeizhangdoc@yeah.net

### References

- [1] Tu QY, Yang X, Ding BR. Epidemiological survey of vascular dementia after cerebral arterial thrombosis. *Chinese Journal of Gerontology* 2011; 31: 3576-3579.
- [2] Lv LH, Chen YH. The study on the blood fat levels and risk factors about vascular diseases in Alzheimer disease and vascular dementia. *Hebei Medical Journal* 2011; 33: 20-21.
- [3] Eom S, Lee C. Functionings of intronic nucleotide variants in the gene encoding pleckstrin homology like domain beta 2 (PHLDB2) on susceptibility to vascular dementia. *World J Biol Psychiatry* 2013; 14: 227-32.
- [4] Li HM. Analysis of influence factor of vascular dementia after cerebral arterial thrombosis. *China Medical Herald* 2015; 3: 230-232.
- [5] Liu YM, Zhang CD. Analysis of relative factor of vascular dementia after cerebral arterial thrombosis. *Chinese Practical Journal of Rural Doctor* 2013; 20: 54-56.
- [6] Pan HF, Qu F. Risk factors of vascular dementia after cerebral arterial thrombosis. *Modern Journal of Integrated Traditional Chinese and Western Medicine* 2011; 20: 2662-2663.
- [7] Stasiak A, Mussur M, Unzata M, Lazewska D, Kiec-Kononowicz K, Fogel WA. The central histamine level in rat model of vascular dementia. *J Physiol Pharmacol* 2011; 62: 549-58.
- [8] Zhu HY, Xiao SP, Sun HY. Correlation between Activity of Butyrylcholinesterase and White Matter Lesions in Patients with Vascular Dementia. *Chinese General Practice* 2013; 16: 2257-2259.
- [9] Lee AY. Vascular dementia. *Chonnam Med J* 2011; 47: 66-71.
- [10] Lu HL, Yang JF, Xu YK. Analysis of risk factors and imaging display in vascular dementia. *Hebei Medical Journal* 2011; 33: 383-384.
- [11] Kim HJ, Moon WJ, Han SH. Differential cholinergic pathway involvement in Alzheimer's disease and subcortical ischemic vascular dementia. *J Alzheimers Dis* 2013; 35: 129-36.
- [12] Du J, Ma M, Zhao Q, Fang L, Chang J, Wang Y, Fei R, Song X. Mitochondrial bioenergetics deficits in the hippocampi of rats with chronic ischemia-induced vascular dementia. *Neuroscience* 2013; 231: 345-52.
- [13] Xing Y, Qin W, Li F, Jia XF, Jia J. Association between sex hormone and cognitive and neuropsychiatric manifestations in vascular dementia (VaD). *Arch Gerontol Geriatr* 2013; 56: 85-90.
- [14] Feng LJ, Zhang N, Cheng Y, et al. Cognitive functions and behavioral and psychological

## Correlation of WML and LI

- symptoms in patients with Alzheimer's disease and patients with vascular dementia. *Chinese Mental Health Journal* 2011; 25: 334-338.
- [15] Yang YS, Liu ZD, Zhang J. Study on the difference of depression in alzheimer's disease and depression in vascular dementia. *J Clin Exp Med* 2013; 12: 1196-1198.
- [16] Sharma B, Singh N. Behavioral and biochemical investigations to explore pharmacological potential of PPAR-gamma agonists in vascular dementia of diabetic rats. *Pharmacol Biochem Behav* 2011; 100: 320-9.
- [17] Brodtmann A. IJS announces journal series on stroke,cognition and vascular dementia. *Int J Stroke* 2011; 6: 375.
- [18] Bjerke M, Zetterberg H, Edman A, Blennow K, Wallin A, Andreasson U. Cerebrospinal fluid matrix metalloproteinases and tissue inhibitor of metalloproteinases in combination with sub-cortical and cortical biomarkers in vascular dementia and Alzheimer's disease. *J Alzheimers Dis* 2011; 27: 665-76.
- [19] Batty GD, Li Q, Huxley R, Zoungas S, Taylor BA, Neal B, de Galan B, Woodward M, Harrap SB, Colagiuri S, Patel A, Chalmers J; VANCE Collaborative group. Oral disease in relation to future risk of dementia and cognitive decline: prospective cohort study based on the Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified-Release Controlled Evaluation (ADVANCE) trial. *Eur Psychiatry* 2013; 28: 49-52.
- [20] Racic D, Slankamenac P, Vujkovic Z, Miljković S, Dajić V, Kovacević AD. Vascular dementia: clinical and neuroradiological correlation. *Med Pregl* 2011; 64: 152-6.
- [21] Yang L, Qin QB. Research progress on mild cognitive impairment and its risk factors. *The Journal of Practical Medicine* 2011; 27: 2303-2305.
- [22] Zhao YW, Qu Y, Fang NY. Progress in the clinical research of mild cognitive impairment in the elderly. *Geriatrics & Health Care* 2010; 16: 125-128.